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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/22/2002 /C

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/945,254	MEYERS ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-33, 38-39, 42-48* is/are rejected.

7)☒ Claim(s) *34-37,40 and 41* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 August 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Claims 32-48 are now pending and under consideration in this application.

Election/Restrictions

Applicant's election without traverse of Group VI, original claims 23-24 (applicants have cancelled all original claims 1-31 and filed new claims 32-38 directed to the elected group) in Paper No. 8 is acknowledged.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Information Disclosure Statement

Applicants' submission of a number of GenBank documents in the IDS is acknowledged. However, Examiner has not considered all of them because applicants have failed to provide the name of the author, and the date of the publications. In order to consider those documents, Examiner urges applicants to provide the name of the author and the date of publication of each of the document in a separate form 1449.

Specification

The disclosure is objected to because of the following informalities: The specification contains blank spaces in several pages (for example page 11, 12 etc.). Examiner urges the applicants to fill up those blank spaces with the appropriate information on the above pages and in all other pages where the blanks occurs in order to overcome this objection. Appropriate correction is required.

Claim Objections

Claims 37 and 41 are objected to because of the following informalities: Claims 37 and 41 recite an abbreviation "HGT-1". Examiner requests applicants to expand the abbreviation at least in the first occurrence of the abbreviation. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32, 33, 38, 39, 42, 46 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the method of determining whether the polypeptide has bound to the test compound. While the claims recite that it will be determined whether the compound binds to polypeptide or not, it does not disclose the essential steps involved in that method of determination.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a compound which binds to a polypeptide comprising the amino acid sequence SEQ ID NO: 2, does not reasonably provide enablement for a method of identifying a compound which binds to a polypeptide comprising any contiguous 10 amino acids of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 42-45 are so broad as to encompass any human galactosyltransferase (HGT) comprising 10 consecutive amino acids of SEQ ID NO: 2. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of HGTs broadly encompassed by the claims including variants, mutants and recombinants. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid

sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single HGT.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any HGT which matches only to any 10 contiguous amino acids with SEQ ID NO:2 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting HGT activity; (B) the general tolerance of human HGTs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any human HGT amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope

of the claims broadly including all or any human HGT with an enormous number of amino acid modifications of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of binding agents that bind to any or all HGTs is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 42-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 42-45 are directed to a method of identifying binding agents to polypeptide fragments (corresponding to 10 contiguous amino acid portions) of SEQ ID NO:2. Claims 42-45 are rejected under this section of 35 USC 112 because the claims are directed to a method using a genus of polypeptide fragments of SEQ ID NO:2 that have not been disclosed in the specification. No description has been provided of the polypeptide fragment sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:2 has been provided by applicants, which would indicate that they had possession of the claimed genus of fragment polypeptides. The specification does not contain any disclosure of the function of all the polypeptide sequences derived from SEQ ID NO:2, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides, which can have a wide variety of functions (i.e., peptides which may

have HGT-1 activity, high activity, low activity or no activity at all). Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 46-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 46-48 are directed to a method of determining binding agents, which bind to allelic variants of SEQ ID NO:2 encoded by a genus of DNA molecules, which hybridize to SEQ ID NO:1 or 3 under stringent conditions.

The specification defines an "allelic sequence" as natural sequence occurring at the same locus on the chromosome. The art defines the allelic variant as an alternative form of the gene, which may result in at least one mutation in the nucleic acid sequence. Alleles may result in altered mRNAs or polypeptides whose structure or function may or may not be altered. This definition does not provide any specific information about the structure of naturally occurring (alleles) variants of SEQ ID NO:2 (i.e. where are the regions within which mutations are likely to

occur) nor discloses any function for naturally occurring variants. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO:2 relates to the structure of any naturally occurring alleles. The general knowledge in the art concerning alleles dose not provide any indication of how one allele is representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art, structure of one does not provide guidance to the structure of others. The genus of polypeptides (allelic variants of SEQ ID NO:2) encoded by above DNAs comprises a large variable genus with potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus (i.e. the sequence encoding SEQ ID NO:2), which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piller et al. (J. Biol.Chem., 1983, Vol. 258(20):12293-12299) or Isshiki et al. (J. Biol.Chem., 1999, Vol. 274, 12499-12507) or Amado et al. (J. Biol.Chem., 1998, Vol. 272(21):12770-12778) or Conklin et al. (US 6,361,985, 3-2002) and the common knowledge in the art of biochemistry. Claims 46-48 in this instant application are drawn to a method of identifying binding agents to allelic variants of the polypeptide with SEQ ID NO:2 by performing a human galactosyltransferase activity assay.

Piller et al., Isshiki et al. or Amado et al. or Conklin et al. teach the isolation and, characterization and cloning (except for Piller et al.) of a novel human galactosyltransferase. The references also teach activity assays for those galactosyltransferases. However, it is not clear whether the reference human galactosyltransferases have the same amino acid sequence as that of SEQ ID NO:2 in the instant application. (Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594). The references also do not explicitly teach an assay for determining binding agents, except for the reference of Conklin et al. which in fact teaches binding agents which binds to the human galactosyltransferase taught in that reference (see column 4, 5th para). Since all the references teach galactosyltransferase

from humans, Examiner has taken the position that the reference HGTs are all allelic variants of SEQ ID NO:2.

Therefore, with all the above references in hand which teach HGT activity assays (and also one reference which actually teaches a binding agent which binds to said HGT) it would have been obvious to one of ordinary skill in the art to combine such teachings with the general knowledge in the art regarding setting up a direct binding assay, competitive binding assays and/or yeast 2-hybrid assays, and develop an assay to identify a binding agent. One of ordinary skill in the art would have been motivated to do so as the above references teach the importance of the above enzymes in human physiology and cellular regulation. One of ordinary skill in the art would have a reasonable expectation of success since the art teaches in general, many ways of setting up binding assays and thc above references teach novel HGTs.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

Claims 34-37, 40-41 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Manjunath N. Rao Ph.D.

10/21/02